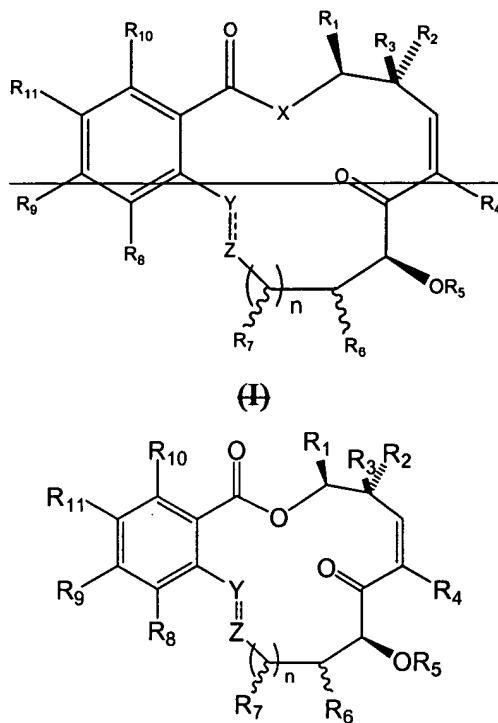


AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or pharmaceutically acceptable derivative thereof;

wherein **R₁** is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

R₂ and **R₃** are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

R₁ and **R₂**, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or

R₁ and **R₃**, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

R₄ is hydrogen or halogen;

R₅ is hydrogen, an oxygen protecting group or a prodrug;

R₆ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R₇, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R₈ is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR₁₂, or NR₁₂R₁₃;

R₉ is hydrogen, halogen, ~~hydroxyl, protected hydroxyl, OR₁₂, SR₁₂, NR₁₂R₁₃, -X₁(CH₂)_pX₂-R₁₄~~, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X₁(CH₂)_pX₂-R₁₄;

wherein R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R₁₂ and R₁₃, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R₁₂ and R₁₃ are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X₁ and X₂ are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X₂-R₁₄ together are N₃ or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R₁₄ is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is -(C=O)NHR₁₅ -(C=O)OR₁₅, or -(C=O)R₁₅, wherein each occurrence of R₁₅ is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R₁₄ is -SO₂(R₁₆), wherein R₁₆ is an aliphatic moiety, wherein one or more of R₁₄, R₁₅, or R₁₆ are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R₈ and R₉ may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted

with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R₁₀ is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R₁₁ is hydrogen, hydroxyl or protected hydroxyl;

~~X is absent or is O, NH, N-alkyl, CH₂ or S;~~

Y is CHR_{17} , $\text{O}-\text{C}=\text{O}$, CR_{17} or NR_{17} ; and **Z** is CHR_{18} , O , $\text{C}=\text{O}$, CR_{18} or NR_{18} , wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken together is $-\text{O}-$, $-\text{CH}_2-$ or $-\text{NR}_{19}-$, wherein R_{19} is hydrogen or lower alkyl, and **Y** and **Z** may be connected by a single or double bond; and

a pharmaceutically suitable carrier or diluent.

wherein the compound is present in an amount effective to inhibit production of a pro-inflammatory and/or immunologic cytokine.

2. (Currently Amended) The composition of claim 1, wherein:

R₁ is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R₂ and **R₃** are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R₁ and **R₂**, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen; or

R₁ and **R₃**, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R₄ is hydrogen or halogen;

R₅ is hydrogen or a protecting group;

R₆ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R₇, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R₈ is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or lower alkyl optionally substituted with hydroxyl, protected hydroxyl, SR₁₂, or NR₁₂R₁₃;

R₉ is hydrogen, halogen, ~~hydroxyl, protected hydroxyl, OR₁₂, SR₁₂, NR₁₂R₁₃, -X₁(CH₂)_pX₂-R₁₄~~, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X₁(CH₂)_pX₂-R₁₄;

wherein R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, lower alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or a protecting group, or R₁₂ and R₁₃, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R₁₂ and R₁₃ are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X₁ and X₂ are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X₂-R₁₄ together are N₃ or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R₁₄ is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is -(C=O)NHR₁₅ -(C=O)OR₁₅, or -(C=O)R₁₅, wherein each occurrence of R₁₅ is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or R₁₄ is -SO₂(R₁₆), wherein R₁₆ is an alkyl moiety, wherein one or more of R₁₄, R₁₅, or R₁₆ are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R₈ and **R₉** may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

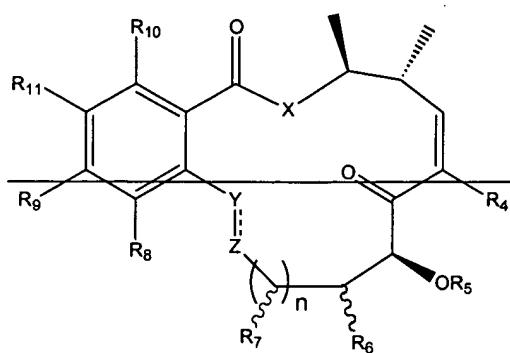
R₁₀ is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

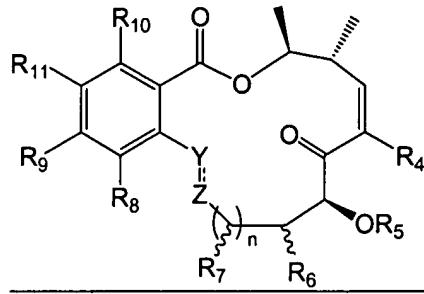
R₁₁ is hydrogen, hydroxyl or protected hydroxyl;

~~X is absent or is O, NH, N-alkyl, CH₂ or S;~~

Y is CHR₁₇, O, C=O, CR₁₇ or NR₁₇; and Z is CHR₁₈, O, C=O, CR₁₈ or NR₁₈, wherein each occurrence of R₁₇ and R₁₈ is independently hydrogen or lower alkyl, or R₁₇ and R₁₈ taken together is -O-, -CH₂- or -NR₁₉-, wherein R₁₉ is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond.

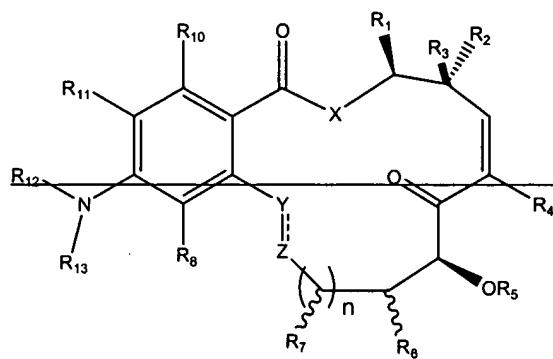
3. (Currently Amended) The composition of claim 2, where ~~X is oxygen and n is 1.~~
4. (Original) The composition of claim 2, where R₄ is halogen.
5. (Original) The composition of claim 2, where R₄ is fluorine.
6. (Original) The composition of claim 2, where Y and Z together represent -CH=CH-
7. (Original) The composition of claim 2, where Y and Z together represent trans -CH=CH-
8. (Currently Amended) The composition of claim 2, wherein R₁ and R₂ are each methyl and R₃ is hydrogen and the compound has the structure:

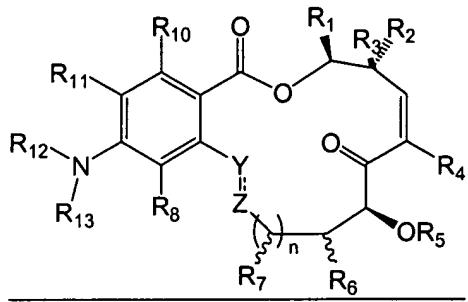




wherein R₄-R₁₁, n, X, Y and Z are as defined in claim 2.

9. (Currently Amended) The composition of claim 8, wherein X is oxygen and n is 1.
10. (Original) The composition of claim 8, wherein R₄ is halogen.
11. (Original) The composition of claim 8, wherein Y and Z together represent -CH=CH-.
12. (Currently Amended) The composition of claim 8, wherein X is oxygen, n is 1, R₄ is halogen and Y and Z together represent -CH=CH-.
13. (Original) The composition of claim 11 or 12 wherein -CH=CH- is *trans*.
14. (Currently Amended) The composition of claim 2, wherein R₉ is NR₁₂R₁₃ and the compound has the structure:

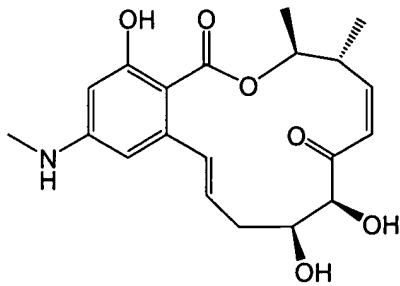




wherein $\underline{R_4-R_{12}}$, \underline{n} , \underline{X} and \underline{Z} $\underline{R_1-R_{13}}$, \underline{n} , \underline{Y} and \underline{Z} are as defined in claim 2, or

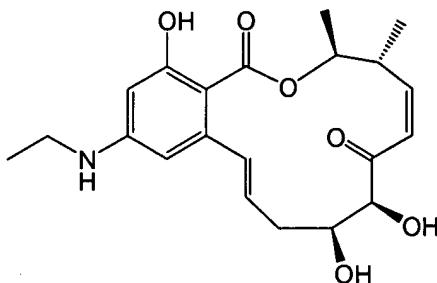
R_{13} and R_8 may, when taken together, form a cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydrogen, alkyloxy, amino, alkylamino, aminoalkyl, and halogen.

15. (Currently Amended) The composition of claim 14, wherein \underline{X} is oxygen and n is 1.
16. (Original) The composition of claim 14, wherein R_4 is halogen.
17. (Original) The composition of claim 14, wherein Y and Z together represent $-CH=CH-$.
18. (Original) The composition of claim 14, wherein R_1 and R_2 are each methyl and R_3 is hydrogen.
19. (Currently Amended) The composition of claim 14, wherein \underline{X} is oxygen, n is 1, R_1 and R_2 are each methyl, R_3 is hydrogen, R_4 is halogen, and Y and Z together represent $-CH=CH-$.
20. (Original) The composition of claim 17 or 19, wherein $-CH=CH-$ is trans.
21. (Original) The composition of claim 1 wherein the compound has the structure:



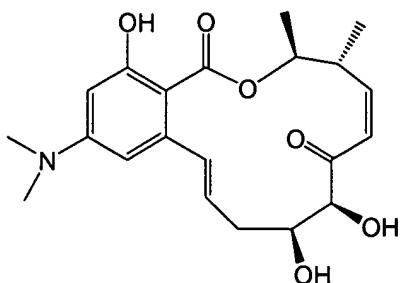
or pharmaceutically acceptable derivative thereof.

22. (Original) The composition of claim 1 wherein the compound has the structure:



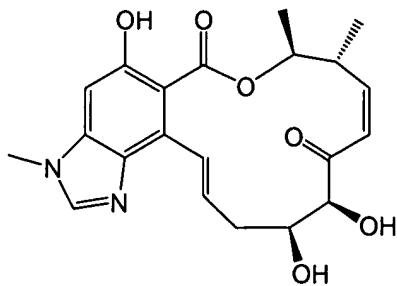
or pharmaceutically acceptable derivative thereof.

23. (Original) The composition of claim 1 wherein the compound has the structure:



or pharmaceutically acceptable derivative thereof.

24. (Original) The composition of claim 1 wherein the compound has the structure:

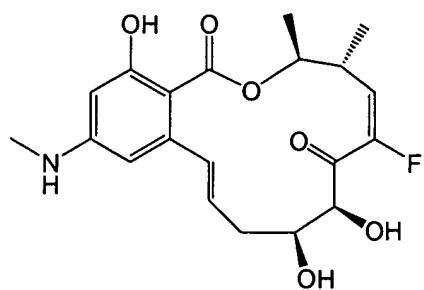


or pharmaceutically acceptable derivative thereof.

25. (Canceled)

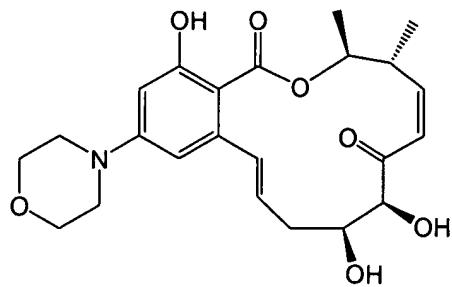
26. (Canceled)

27. (Original) The composition of claim 1 wherein the compound has the structure:



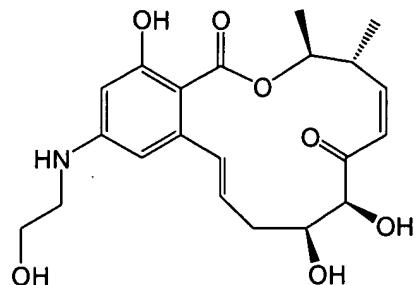
or pharmaceutically acceptable derivative thereof.

28. (Original) The composition of claim 1 wherein the compound has the structure:



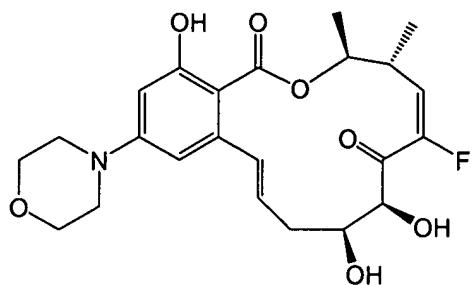
or pharmaceutically acceptable derivative thereof.

29. (Original) The composition of claim 1 wherein the compound has the structure:



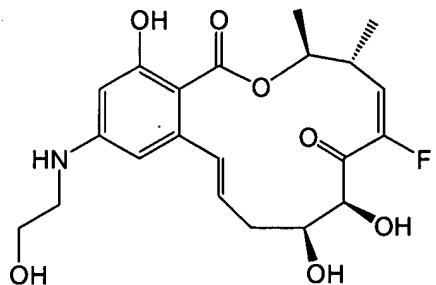
or pharmaceutically acceptable derivative thereof.

30. (Original) The composition of claim 1 wherein the compound has the structure:



or pharmaceutically acceptable derivative thereof.

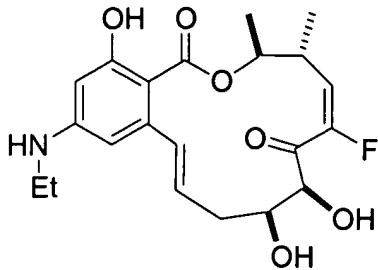
31. (Original) The composition of claim 1 wherein the compound has the structure:



or pharmaceutically acceptable derivative thereof.

32. (Canceled)

33. (Original) The composition of claim 1 wherein the compound has the structure:



or pharmaceutically acceptable derivative thereof.

34. (Canceled)

35. (Canceled)

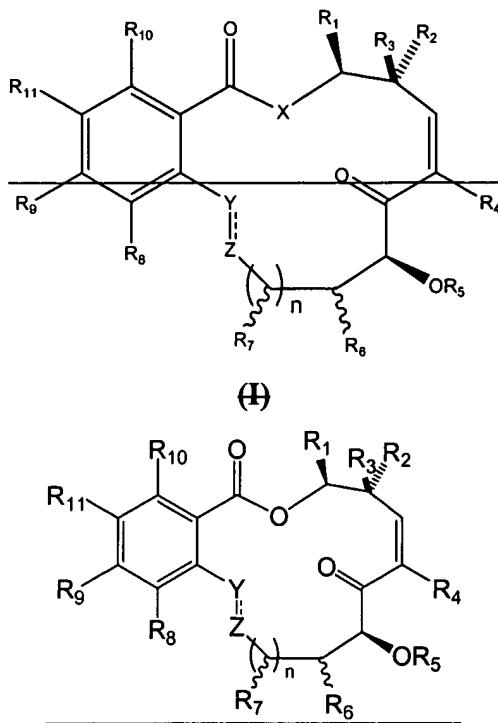
36. (Original) The pharmaceutical composition of claim 1, wherein the composition is for oral administration.

37. (Canceled)

38. (Currently Amended) The pharmaceutical composition of claim 37 of claim 1, wherein the pro-inflammatory and/or immunologic cytokine is TNF α , IL-1, IL-6, IL-8 or IL-2.

39. (Currently Amended) A method for treating an inflammatory and/or autoimmune disorder rheumatoid arthritis, psoriasis, asthma, sepsis, inflammatory bowel disease, atopic dermatitis or Crohn's disease comprising:

systemically administering to a subject in need thereof a pharmaceutically suitable carrier or diluent and a therapeutically effective amount of a compound having the structure:



or pharmaceutically acceptable derivative thereof;

wherein **R₁** is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

R₂ and **R₃** are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

R₁ and **R₂**, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or

R₁ and **R₃**, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

R₄ is hydrogen or halogen;

R₅ is hydrogen, an oxygen protecting group or a prodrug;

R₆ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R₇, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R₈ is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, **SR₁₂**, or **NR₁₂R₁₃**;

R₉ is hydrogen, halogen, ~~hydroxyl, protected hydroxyl, OR₁₂, SR₁₂, NR₁₂R₁₃, - X₁(CH₂)_pX₂-R₁₄~~, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X₁(CH₂)_pX₂-R₁₄;

wherein R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R₁₂ and R₁₃, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R₁₂ and R₁₃ are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X₁ and X₂ are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X₂-R₁₄ together are N₃ or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R₁₄ is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is -(C=O)NHR₁₅ -(C=O)OR₁₅, or -(C=O)R₁₅, wherein each occurrence of R₁₅ is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R₁₄ is -SO₂(R₁₆), wherein R₁₆ is an aliphatic moiety, wherein one or more of R₁₄, R₁₅, or R₁₆ are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R₈ and R₉ may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R₁₀ is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R₁₁ is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N alkyl, CH₂ or S;

Y is CHR₁₇, O, C=O, CR₁₇ or NR₁₇; and Z is CHR₁₈, O, C=O, CR₁₈ or NR₁₈, wherein each occurrence of R₁₇ and R₁₈ is independently hydrogen or aliphatic, or R₁₇ and R₁₈ taken

together is $-O-$, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond; and

a pharmaceutically suitable carrier or diluent.

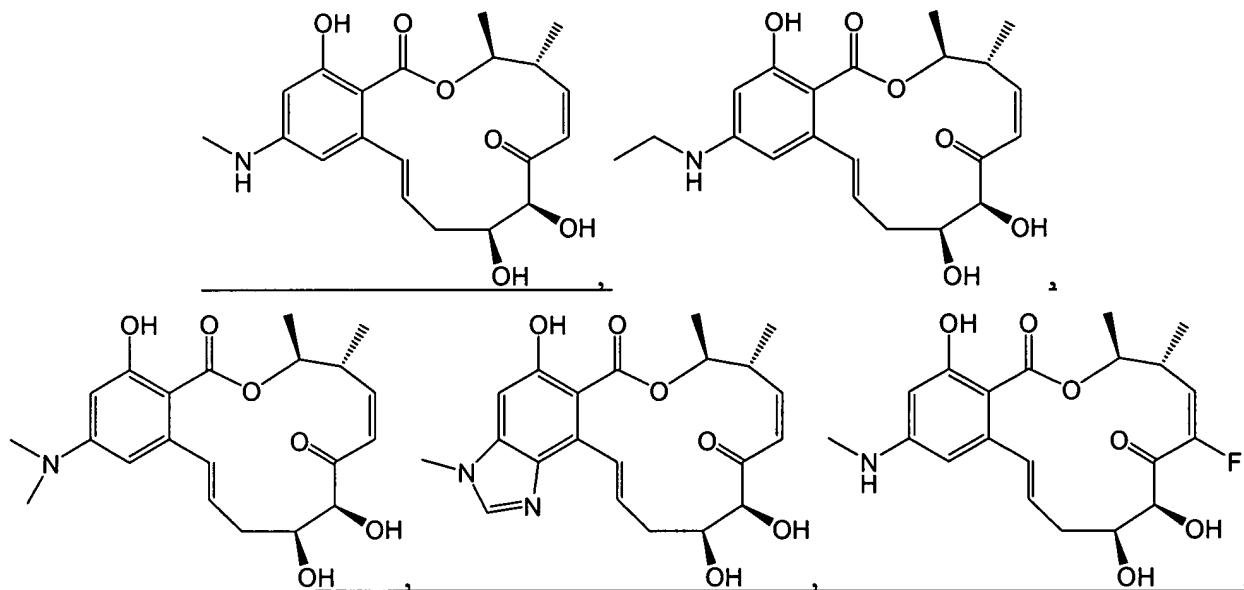
wherein the compound is present in an amount effective to inhibit production of a pro-inflammatory and/or immunologic cytokine.

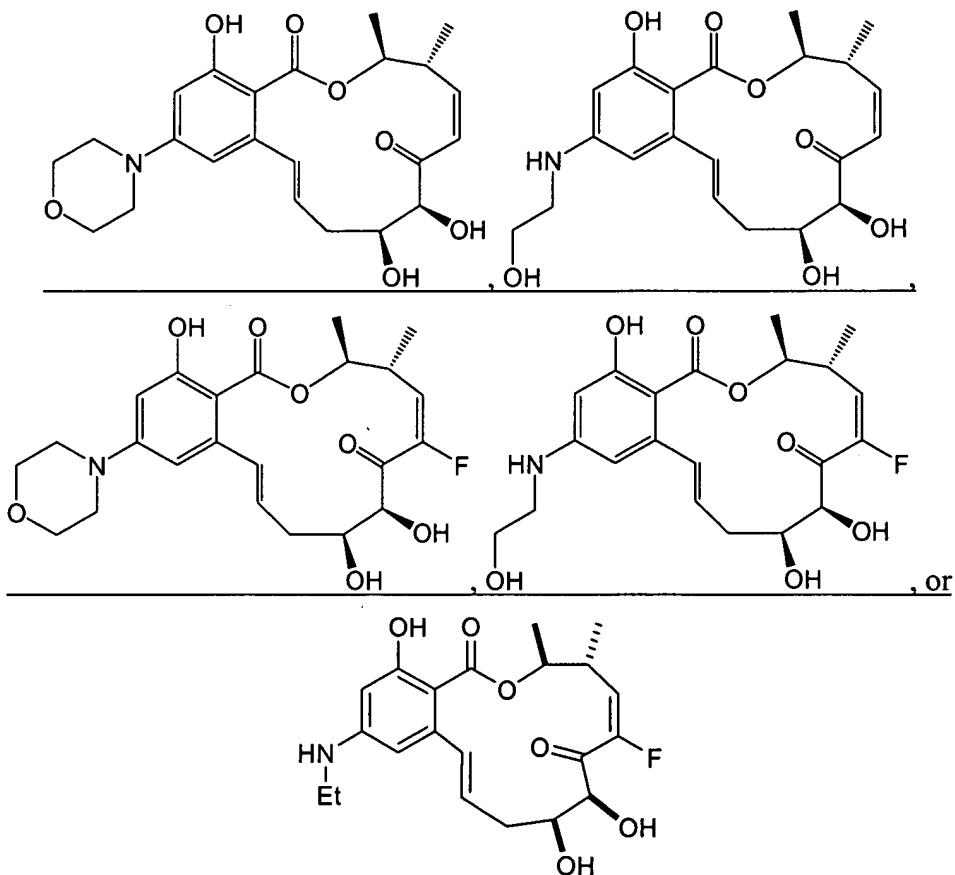
40. (Original) The method of claim 39, wherein the compound is administered orally.

41. (Canceled)

42. (Currently Amended) The method of ~~claim 41~~ claim 39, wherein the method is for treating psoriasis.

43. (Currently Amended) The method of claim 41, wherein ~~the compound has the structure~~
the compound has any one of the following structures:





or pharmaceutically acceptable derivative thereof.

44. (Canceled)

45. (Currently Amended) The method of ~~claim 44~~ claim 39, wherein the pro-inflammatory and/or immunologic cytokine is TNF α , IL-1, IL-6, IL-8 or IL-2.